

ORIGINAL RESEARCH

# Bovine Arch and Stroke Laterality

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**BACKGROUND:** Left-hemispheric strokes are more frequent and often have a worse outcome than their right-hemispheric counterparts. This study aimed to evaluate whether cardioembolic stroke laterality is affected by anatomical characteristics of the aortic arch. We hypothesized that laterality varies between patients with bovine versus standard arch.

**METHODS AND RESULTS:** We retrospectively identified 1598 acute cardioembolic strokes in patients with atrial fibrillation from our institutional stroke database (2009–2017). Inclusion criteria were acute anterior circulation ischemic infarct and availability of both arch and brain imaging (magnetic resonance imaging or computed tomography). Alternative causes of stroke and anomalous arch were excluded. Imaging was reviewed for stroke characterization and laterality and arch branching pattern. Bovine arch denotes a common origin of the brachiocephalic trunk and left common carotid artery. Strokes were classified as bilateral (left or right). Univariate analysis was performed using chi-square tests. The final cohort comprised 615 patients, mean age 77 years (SD 11.8 years) with 376 women (61%) and 33% white, 30% black, and the remainder mixed/Hispanic. Standard arch (n=424) stroke distribution was left 43.6% (185), right 45.1% (191), and bilateral 11.3% (48). Bovine arch (n=191) stroke distribution was left 51.3% (98), right 35.6% (68), and bilateral 13.1% (25). Bovine arches were associated with more left-sided strokes compared with standard arches ( $P=0.018$ ). There was an association between black race and bovine arch ( $P=0.0001$ ).

**CONCLUSIONS:** Bovine aortic arch configuration is associated with left hemispheric laterality of cardioembolic stroke. This study enriches the understanding that arch anatomy influences stroke laterality and highlights the need for further research into the causative hemodynamic factors.

**Key Words:** aortic arch ■ embolic stroke ■ ischemic stroke

Stroke, the leading cause of disability and the second most common cause of death worldwide, is 90% ischemic in nature.<sup>1</sup> At least 20% of ischemic strokes are directly attributable to high-risk cardiac abnormalities. Another 30%, where the cause cannot be clearly established, are classified as “cryptogenic,” but most of these strokes have embolic features, suggesting a possible cardioaortic origin.<sup>2</sup> Cardioembolic infarction is generally the most severe ischemic stroke subtype, with a low frequency of asymptomatic patients at hospital discharge and high mortality.<sup>3,4</sup>

Left-hemispheric ischemic strokes are overall more frequent and are often associated with a worse outcome than their right-hemispheric counterparts.<sup>5</sup> However, there are conflicting reports as to the left-right propensity of cardioembolic infarcts.<sup>6–8</sup> We

hypothesized that the laterality of cardiogenic cerebral embolization may in part be affected by anatomic characteristics of the great vessel branching pattern of the aortic arch.

The standard aortic arch branching pattern, found in ≈65% of the population,<sup>9</sup> consists of 3 great vessels with separate origins arising from the arch: brachiocephalic, left common carotid, and left subclavian arteries (Figure 1A). The most common variant in the branching pattern of the aortic arch is a common origin of the brachiocephalic and left common carotid arteries. The reported prevalence of this branching pattern is ≈13%.<sup>9,10</sup> The second most common arch variant, with an overall rate of 9%,<sup>9,11</sup> occurs when the left common carotid shares a common origin with the brachiocephalic artery, bifurcating at an average distance of

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## CLINICAL PERSPECTIVE

### What Is New?

- Bovine arch configuration is associated with left hemispheric laterality of cardioembolic stroke.

### What Are the Clinical Implications?

- This study highlights the need for further research into whether patients with bovine arch have a worse prognosis, in which case arch anatomy should be factored into decision making regarding anticoagulation in patients at high risk for cardioembolic stroke.

## Nonstandard Abbreviations and Acronyms

<b>CT</b>	computed tomography
<b>NIHSS</b>	National Institutes of Health Stroke Scale

<1 cm from the origin.<sup>11</sup> These aortic arch branching pattern variants have been described in the literature as a “bovine arch” (Figure 1B). The term bovine arch refers to the configuration of the vessels reminiscent (to some) of cattle horns, but bearing no resemblance to the aortic arch branching pattern of cattle.<sup>10,12</sup>

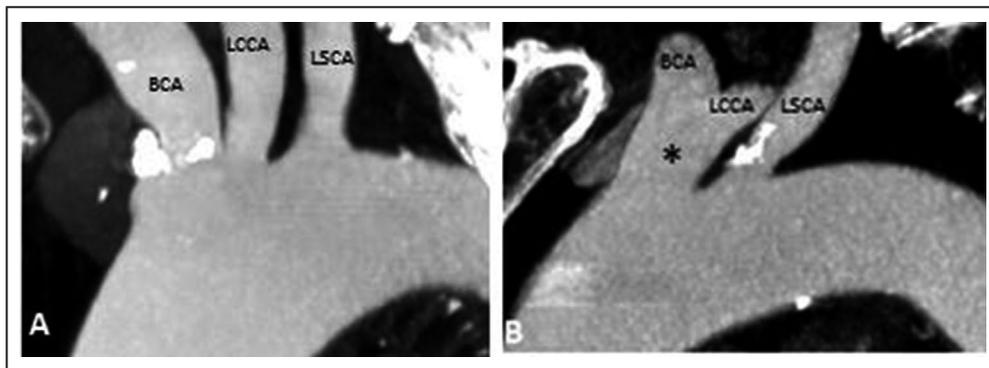
To our knowledge, a retrospective pilot study we previously published<sup>13</sup> was the first to attempt to correlate aortic arch anatomy with stroke laterality in patients at high risk for cardioembolic infarcts. That study demonstrated a trend toward left-sided cardioembolic infarcts in patients with bovine arch compared with standard arch. The purpose of this study, which employed a larger stroke database from a different institution, was to confirm a correlation between aortic arch anatomy and cardioembolic stroke laterality.

## METHODS

The authors declare that all supporting data are available within the article. The study was approved by the Albert Einstein College of Medicine institutional review board. Informed consent was not required because of the retrospective nature of the study.

We retrospectively identified 1598 acute ischemic stroke events in patients with known atrial fibrillation from our institutional stroke database between January 2009 and December 2017. Looking Glass Clinical Analytics (Streamline Health Solutions, LLC) was used to further refine the cohort. For each unique patient, the first stroke event within this timeframe was selected while subsequent events were excluded, yielding 1459 patients. This was done so that each patient represented only a single data point, reducing the possibility of extraneous patient-specific factors influencing the data. All of these patients had brain imaging (either computed tomography [CT; 32%] or magnetic resonance imaging [68%]) at the time of the stroke event, and there was no significant difference in the cohorts between the imaging modality used to diagnose stroke. Those patients who had imaging studies at our institution that included aortic arch architecture (eg, CT of the chest, CT angiogram of the neck, magnetic resonance angiogram of the neck) were identified, yielding 1232 patients.

Imaging review was conducted by a radiology resident with 4 years of experience (J.S.) and by medical students trained to identify aortic arch branching patterns and infarct types (J.M., M.A.). Equivocal aortic arch characterization was decided by consensus in consultation with a board-certified thoracic radiologist with >25 years of experience (L.H.). Equivocal infarct categorization was decided by consensus in consultation with a board-certified neuroradiologist with 13 years of experience (S.S.). Brain imaging was reviewed for characterization of stroke size (lacunar



**Figure 1. Standard and bovine aortic arch anatomy.**

**A**, Reconstructed image from a computed tomography (CT) angiogram of the neck demonstrates a standard configuration of the aortic arch brachiocephalic artery (BCA), left common carotid artery (LCCA), and left subclavian artery (LSCA). **B**, Reconstructed image from a CT angiogram of the neck demonstrates a bovine arch, with a common trunk (\*) for the BCA and LCCA.



**Figure 2.** Flow chart demonstrating the selection of the final study population. A total of 615 patients were included in the study.

versus nonlacunar) and hemispheric laterality (right, left, or bilateral). Multiple acute infarcts in the same hemisphere were considered 1 event. Lacunar infarcts were defined as  $\leq 1.5$  cm in the distribution of perforating vessels of the middle cerebral artery. Aortic arch branching pattern was reviewed blinded to the intracranial findings. For the purposes of this study, the designation of “bovine arch” denotes either a vessel giving rise to both the brachiocephalic and left common carotid arteries, or a common origin of the 2 vessels. Additional data points collected via electronic medical record review included age, sex, ethnicity, and stroke risk factors.

Inclusion criteria were an acute anterior circulation ischemic infarct and availability of imaging of both the aortic arch and brain. Exclusion criteria included atypical arch (not standard or bovine, eg, left arch with aberrant right subclavian artery or right aortic arch), aortic dissection, aortic arch graft, posterior circulation stroke, lacunar infarct only,  $>50\%$  intra-cranial/extracranial carotid stenosis ipsilateral to the stroke, and other causes of stroke (ie, dissection, postendarterectomy). Posterior circulation infarcts were excluded because the bovine arch variant was not expected to affect lateralization of emboli to the vertebral arteries.

## Statistical Analysis

We analyzed the differences in age between the standard and bovine cohorts using Student *t* test. Differences in race and sex between the 2 cohorts were analyzed with Fischer exact test. Pearson chi-square test was used to analyze the association of each cohort with stroke risk factors, stroke laterality, and reperfusion therapy. Additionally, Mantel–Haenszel chi-square test was used to analyze the association of stroke laterality with bovine arch, conditioned on race. For all of these analyses, a *P* value of <0.05 was considered significant.

All statistical analyses were performed using R version 3.6.1 (The R Foundation).

## RESULTS

The final cohort comprised 615 patients (Figure 2), with 376 women (61%) and a mean age of 77.22 years (SD 11.8 years). Race/ethnicity was self-reported as white in 33%, black in 30%, and the remainder in mixed/Hispanic ethnicity. Demographic data and clinical characteristics of the cohorts are summarized in Table 1. The bovine arch cohort was slightly younger than the standard arch cohort (*P*=0.02). Of note, 41% of patients with bovine arch were black and there was a statistically significant association of black race with bovine arch (odds ratio [OR], 2.5; 95% CI, 1.56–3.93 [*P*=0.0001]).

A total of 89% of the cohort had a documented history of hypertension, 28% had coronary artery disease, 38% had type 2 diabetes mellitus, and 44% had

dyslipidemia. There was a significantly increased prevalence of type 2 diabetes mellitus in the bovine arch cohort (*P*=0.02). There were no other significant differences in stroke risk factors between the cohorts. There was no significant association of any of the stroke risk factors with stroke laterality (Table 2).

Standard arch was identified in 424 (69%) patients: left-sided in 43.6% (185), right-sided in 45.1% (191), and bilateral in 11.3% (48). Bovine arch was identified in 191 (31%) patients: left-sided in 51.3% (98), right-sided in 35.6% (68), and bilateral in 13.1% (25). Bovine arches were associated with more left-sided strokes compared with standard arches (OR, 1.57; 95% CI, 1.09–2.24 [ $\chi^2=5.61$ ], *P*=0.018). Stroke laterality in standard and bovine arches is summarized in Table 3.

## DISCUSSION

The primary finding of this study is that there is a significant propensity for left-hemispheric cardioembolic infarcts in patients with bovine aortic configuration compared with those with a standard aortic arch, confirming our hypothesis. In general, left-hemispheric strokes are associated with a higher admission National Institutes of Health Stroke Scale (NIHSS) and increased mortality compared with their right-hemispheric counterparts.<sup>5</sup>

There is no gold standard for diagnosing cardioembolic stroke. The diagnosis depends on circumstantial evidence provided by detection of a potential major cardiac source of embolism in the absence of significant ipsilateral arterial disease, as well as supportive clinical, neuroimaging, or laboratory features.

**Table 1. Demographic and Clinical Characteristics in Bovine and Standard Arches**

	Standard	Bovine	<i>P</i> Value
Age average (SD), y	77.9 (11.7)	75.6 (12)	0.02*
Sex, No. (%)			
Women	255 (60)	121 (63)	0.48
Men	169 (40)	70 (37)	
Race, No. (%)			
Black	103 (24)	78 (41)	0.0001*
White	157 (37)	48 (25)	
Stroke risk factors, No. (%)			
Hypertension	377 (88.9)	173 (90.6)	0.77
Type 2 diabetes mellitus	149 (35.3)	87 (45.5)	0.02*
Smoking	24 (5.7)	12 (6.3)	0.85
Dyslipidemia	189 (44.6)	81 (42.4)	0.60
Coronary artery disease	81 (42.4)	50 (26.2)	0.06
Reperfusion therapy, No. (%)			
Mechanical thrombectomy	58 (13.68)	26 (13.61)	0.98

\*Statistically significant at *P*<0.05.

**Table 2. Stroke Laterality in Demographic and Clinical Cohorts**

	Right	Left	<i>P</i> Value
Sex, No. (%)			
Women	149 (39.6)	184 (48.9)	0.09
Men	110 (46.3)	99 (41.1)	
Race, No. (%)			
Black	81 (44.5)	77 (42.3)	0.12
White	77 (37.6)	103 (50.2)	
Stroke risk factors, No. (%)			
Hypertension	230 (41.9)	252 (45.9)	0.93
Type 2 diabetes mellitus	102 (43.2)	102 (43.2)	0.54
Smoking	16 (44.4)	15 (41.7)	0.66
Dyslipidemia	114 (42.2)	123 (45.6)	0.90
Coronary artery disease	79 (45.7)	72 (41.5)	0.22
Reperfusion therapy, No. (%)			
Mechanical thrombectomy	38 (45.2)	35 (41.7)	0.43

**Table 3. Stroke Laterality in Bovine and Standard Arches**

	Standard, No. (%)	Bovine, No. (%)	Odds Ratio (95% CI)	P Value
Left-sided infarct	185 (43.6)	98 (51.3)	1.57 (1.09–2.24)	0.018*
Right-sided infarct	191 (45.1)	68 (35.6)		

\*Statistically significant at  $P < 0.05$ .

There are numerous high-risk cardioembolic conditions, such as recent myocardial infarction, mechanical heart valve, and dilated cardiomyopathy. For the purpose of simplicity, we limited our patient cohort to those with atrial fibrillation, the most common cause of cardioembolic stroke.<sup>14</sup> To avoid the potential ambiguity of arterial disease as a source of embolism, we excluded patients with significant ipsilateral carotid atheroma.

It stands to reason that laterality of cardioembolic infarcts is affected by anatomical and rheological characteristics of the aortic arch. Prior computer-based 3-dimensional simulation models of medium embolic particles ( $\approx 1$  mm diameter) arising from the heart demonstrated a propensity to travel along the outer curvature of the aorta, perhaps as a result of the aortic curvature and pulsatile nature of aortic blood flow.<sup>15</sup> These particles had a higher tendency to enter aortic branch arteries, rather than continue into the descending aorta, as would be predicted based on volumetric flow alone. In a standard arch, the brachiocephalic artery is the first aortic arch branch, has the largest ostium, and courses cephalad and parallel to the direction of the ascending aorta. Embolic particles would therefore have a higher propensity to enter the brachiocephalic artery (which supplies the right common carotid and right subclavian) rather than the left common carotid artery, which arises second from the arch and has a perpendicular orientation to the arch. This is borne out by our data that demonstrated more than a 50% chance of a right-sided cardioembolic infarct in patients with standard arch. In a bovine arch, where both the brachiocephalic and left common carotids arise from a common trunk or share a common origin, the left common carotid orientation is better aligned with the trajectories of incoming emboli. In addition, once an embolus enters the brachiocephalic artery, it may be transported to either the right subclavian or right common carotid arteries. These 2 factors may contribute to an increased propensity of left-sided cardioembolic infarcts in patients with a bovine arch.

There was an increased prevalence of type 2 diabetes mellitus in the bovine cohort. However, this is likely because of the higher prevalence of type 2 diabetes mellitus in the black population. More importantly, type 2 diabetes mellitus was not associated with stroke laterality and therefore should not be considered as a

potential confounder for the association between bovine arch and stroke laterality.

The overall prevalence of bovine arch variants in our study population (31%) is similar to our pilot study and to that published in the literature for the general population based on chest CT angiography.<sup>10</sup> Our cohort self-identified as 30% black. A number of cadaveric studies have demonstrated a high incidence of bovine aortic arch in blacks.<sup>9,11</sup> This finding was confirmed in our study, which demonstrated a statistically significant association of black race with bovine arch.

### Study Limitations

Our study had several limitations, including its retrospective design and partial reliance on CT imaging for acute stroke detection in a small percentage of patients. Multiple acute infarcts in the same hemisphere were considered 1 event, whereas in reality these may arise from distinct embolic episodes. Although we mitigated against the possibility of carotid artery-to-artery embolic infarcts in our cohort by excluding patients with significant atheroma, it is possible that a small percentage of patients had atherothrombotic strokes arising from the aortic arch. Specifically, we did not exclude patients with extensive aortic atheroma as the arch imaging was often not performed at the time of the stroke. Additionally, we did not assess the size of the infarct; however, the primary outcome is the relationship between arch anatomy and stroke laterality (not size or severity). This is an important topic for future research now that the primary hypothesis has been upheld. Last, our study did not evaluate clinical stroke scales such as the NIHSS, nor did it assess clinical outcomes, which were beyond the scope of this study and may be of interest in future research.

### CONCLUSIONS

This study provides insight on the relationship between aortic arch anatomy and hemispheric lateralization of cardioembolic strokes. There is a significant predilection of emboli to the left cerebral hemisphere in patients with bovine arch, found in  $\approx 30\%$  of the general population. Because left-sided infarcts have a worse overall prognosis, further studies are needed to determine whether patients with bovine arch have a worse prognosis compared with

standard anatomy, in which case arch anatomy should be factored into decision making regarding anticoagulation in patients at high risk for cardioembolic stroke.

## ARTICLE INFORMATION

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### Disclosures

Dr. Haramati's spouse is a board member for Kryon Systems Ltd. The remaining authors have no disclosures to report.

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